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EXAMINER	
MCGARRY, SEAN	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/660,568
Filing Date: September 11, 2000
Appellant(s): RALPH ET AL.

Gina Shishima
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 12/28/04.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct. No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection is correct.

(7) Claims Appendix

A substantially correct copy of the appealed claims appear in the Appendix to the appellant's brief. The minor errors are as follows: In claim 9, line 2, it appears that appellant inserted an extra colon.

(8) Evidence Relied Upon

No evidence is relied upon by the examiner in the rejection of the claims under appeal.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-20 and 64 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The instant invention is broadly drawn to the detection of disease markers expressed in peripheral blood and diagnosing a disease state via the detection. The scope includes the detection of markers for metastatic cancers including breast and prostate cancers but is so broad as to read on the detection of any disease state. The specification, as filed, discloses 7 "markers" (nucleic acid sequences) associated with metastatic prostate cancer that are expressed in peripheral blood of prostate cancer patients. The specification also identifies IL-8 and IL-10 expression in peripheral blood to be associated with metastatic prostate cancer. The specification provides no other examples of any other diseases that may be associated with these 7 species and further provides no other marker genes specifically associated with any particular gene for use in the instantly claimed invention.

With the exception of the markers indicated above the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides markers

required to perform the instant methods regardless of the complexity or simplicity of the method of isolation. The instant specification does not provide "markers" other than those indicated above and one in the art, based on the structure of those would not be able to envision the structure (sequence) of any other "markers" (mRNA) that may be associated with any particular disease within the broad scope of diseases considered in the instant invention. Without a description of such markers, one in the art would not be able to produce primers or probes for any particular marker associated with any particular disease, for example. The specification further does not provide any other disease states that may be determined via the increase or decrease in expression of the 7 "markers" identified in the specification, for example.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v.*

American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further

information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

The instant specification provides guidance for one in the art to find markers, but does not describe a representative number to show possession of the claimed invention. The markers disclosed in the specification are associated with prostate cancer, which disclosure does not provide a description of markers for breast cancer or any of the vast number of disease states that would be included in a group described as "a human disease state". The instant specification has not provided an adequate written description of any markers for any disease other than metastatic cancer (prostate). The specification fails to describe those marker sequences that the invention requires to be quantified, for example. The detection of IL-10 or SEQ ID NO: 49 have been shown to be associated with metastatic prostate cancer but the specification fails to describe what disease other than metastatic prostate cancer can be detected by quantifying IL-10 or SEQ ID NO: 49 in peripheral blood, for example. The specification fails to provide a correlation between the structure and function of IL-10 or SEQ ID NO: 49 and any other

diseases that may be detected by quantification of their expression in peripheral blood, for example.

The instant invention is based on the detection of markers that are differentially expressed in the peripheral blood in a patient with a disease relative to expression in a normal subject. Although the instant specification provides methods of identifying such markers, a sufficient number of markers have not been described to show possession of the broad scope instantly claimed.

Claims 9-20 and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are rejected for those reasons set forth above. One in the art would clearly require the engagement of vast quantities of trial and error experimentation to determine the markers that may be correlated to the vast range of diseases to be diagnosed in the instant methods.

(10) Response to Argument

Appellant argues that the claimed invention is directed to a **method of detecting** [emphasis provided by appellant] the quantity of a disease marker mRNA in the peripheral blood and comparing the quantity of the disease marker in a sample with

the quantity in a sample with the quantity of the disease marker in normal individual's [peripheral] blood. Appellant asserts the appealed claims do not claim a disease marker, but a method that uses them. The argument appears to be that since the compounds not described are not being claimed no rejection of lack of written description can be made. It would appear that such an argument would represent a semantic distinction without a difference since the compounds not described are clearly needed in order to practice the claimed method.

Appellant argues that method have been provided to identify markers. Again it is pointed out *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Appellant points to page 8, lines 10-27, for support of a description of the invention. It is noted that the specification provides no disclosure of mRNA markers at the cited location. Appellant points to pages 85-92, which pages provide general teachings for RNA detection processes. The cited pages, 85-92, provide no disclosure of any particular markers in the peripheral blood that are correlated to any particular disease. Appellant also points to the examples at pages 100-161, which disclosure comprises those specific markers clearly acknowledged in the rejections in the Official Actions of record.

It is noted that at page 16, lines 26-30, of the specification it is stated; "Disease states that may be detected by the present method include any disease state for which

a marker is known and may include metastatic cancer, particularly metastatic prostate cancer, asthma, lupus. . ." It is the position of the examiner that the only known markers for detection of a disease state via mRNA detection in peripheral blood are those specifically disclosed by appellant and acknowledged in the Official Actions of record. If appellant believes that the prior art provides a sufficient description of other markers for disease states known to be expressed in the peripheral blood such a disclosure would be taken into consideration.

Appellant argues that "[t]he steps of the **diagnostic method** [emphasis in original] are clear. While the claims may encompass the use of compositions not specifically exemplified or identified, the claims require that there is a difference in the expression of the disease marker mRNA relative to. . ." Appellant argues as if the markers are not essential to practicing the method. The compounds[marker mRNAs] are not ancillary to the method claimed but are integral to its practice. Since the markers of the instant invention are clearly needed to practice the invention and the scope of such markers have not been adequately described, the invention itself [i.e. a method of using the markers] has not been described.

Appellant is also directed to University of Rochester v. G.D. Searle & Co., 69USPQ2d (CA FC 2004). One would not know how to make the claimed substance other than by a trial and error process."" Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or

infringing methods from non-infringing methods. . .'[t]he claimed method depends upon finding a compound that selectively inhibits PGHS-2 activity. Without such a compound, it is impossible to practice the claimed method of treatment.'"

Appellant argues that Claim 15 is separately patentable since it includes additional limitations that address the Actions concerns relating to identifying markers for disease. Appellant essentially points out what the claim recites and does not appear to make any specific arguments for separate patentability. Appellant also asserts that the action admits, at pages 5-6 of the final action, that the specification provides adequate written description for prostate cancer. The assertion is made out of context. The Action sated that the specification failed to provide a description of any MARKERS for any disease other than metastatic prostate cancer. The rejection of record indicated that none of the rejected claims had sufficient written description and further the rejection makes clear that those markers shown for metastatic prostate cancer do not provide the basis for one in the art to know the structure of any others. Claim 15 is not limited to the markers indicated as described, for example.

Appellant argues that the office action fails to provide a reasonable basis to question the enablement of the instantly claimed methods. Applicant asserts again that the claims are drawn to a method of detection and not to the markers required to perform the methods. Appellant argues as if the markers are not essential to practicing the method. The compounds[marker mRNAs] are not ancillary to the method claimed but are integral to its practice. Appellant argues also that the invention is enabled and

argues that written description and enablement are distinct and cite *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1114 (Fed. Cir. 1991). It is the position of the examiner, that although distinct, there is overlap within the written description, enablement and best mode requirements of 112, first paragraph. In the instant case there is clearly overlap since one in the art would require the use of markers that have not been described. One cannot use these markers in the claimed invention when such markers have not been described. Appellant merely provided a trial and error method of finding "markers" where no guidance for what might be the structure and to what diseases they might be related and how a "difference" (increase, decrease, how much of increase or decrease, miss expression, different tissues, temporal . . etc) in expression of such undisclosed structures is to be correlated with any particular disease. The combinations contemplated are astronomical and the guidance provided is limited to seven markers all related to one type of disease. One in the art has been left to *de novo* determine all of the correlations, without any specific guidance for any particular diseases. One in the art has not been provided any particular starting point for what they might look for as a marker, but is left to find such by trial and error experimentation where there has been no guidance provided such that one would know how or where to look for markers for any particular disease they might wish to detect or diagnose, for example.

Appellant asserts that the action fails to point out why IL-8 or other disease markers would not be a viable marker for other cancers or disease states. The examiner's position is that in order to make such a determination undue quantities of

experimentation would be required. Appellant now appears to argue that IL-8 is a universal disease state indicator. No support for such an assertion is provided other than the disclosure that it[IL-8 mRNA] is expressed in peripheral blood of patients with metastatic prostate cancer. Appellant does not point to any support for markers shown for any disease other than metastatic prostate cancer. It is noted that appellant asserts that markers have been shown for breast cancer but Appellant does not point to any particular support, for example.

The type of experimentation required to practice the invention more broadly than is exemplified is a factor in the enablement analysis, but is not necessarily dispositive. In this case, the more-or-less standard nature of each type of experiment required to expand the scope of the invention is outweighed by the sheer quantity of experimentation required to practice the full scope of the claims, the unpredictability of the art generally (biotechnology) and the claimed method in particular, and the lack of guidance in the specification regarding the direction in which the experimentation should proceed.

Appellant argues that Claim 15 is separately patentable since it includes additional limitations that address the Actions concerns relating to identifying markers for disease. Applicant essentially points out what the claim recites and does not appear to make any specific arguments for separate patentability. Appellant also asserts that the action admits, at pages 5-6 of the final action, that the specification provides adequate written description for prostate cancer. The assertion is made out of context. The Action sated that the specification failed to provide a description of any MARKERS

for any disease other than metastatic prostate cancer. The rejection of record indicated that none of the rejected claims had sufficient written description and further the rejection makes clear that those markers shown for metastatic prostate cancer do not provide the basis for one in the art to know the structure of any others. Claim 15 is not limited to the markers indicated as described, for example.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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